STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 155477

TO: Devesh Khare **Art Unit:** 1623 **Location:** REM-5C35/5C18 **Serial Number:** 10/667216 **Thursday, July 14, 2005**	**From:** Beverly Shears **Location:** Biotech-Chem Library REM 1A54 **Phone:** 571-272-2528 beverly.shears@uspto.gov

Search Notes

Access DB#_____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester=s full Name: Devesh Khare Examiner #: 77931 Date: 05/19/2005
Art Unit: 1623 Phone Number 272-0653 Serial Number: 10/667,216
Mail Box: Remsen 5C18 and Bldg/Room Location: 5C35 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be search Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: See Bib Data Sheet on e-dan.

Inventors (please provide full names): See Bib Data Sheet on e-dan.

Earliest priority Filing Date: **09/20/2002**

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please carry out a search on the attached claim sheet.

Thank you.

STAFF USE ONLY

Searcher:_____
Searcher Phone #:_____
Searcher Location:_____
Date Searcher Picked Up:_____
Date Completed:_____
Searcher Prep & Review Time:_____
Clerical prep time:_____
Online Time:_____

PTO-1590 (1-2000)

Type of Search

NA Sequence (#)_____
AA Sequence (#)_____
Structure (#) _____
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family_____
Other _____

Vendors and cost where applicable

STN_____
Dialog_____
Questel/Orbit_____
Dr. Link_____
Lexis/Nexis_____
Sequence Systems_____
WWW/Internet_____
Other (specify)_____

1. A heparin fraction consisting of constituents having molecular weights of from about 2,000 to about 4,000 daltons, wherein from about 1% to about 100% of hydroxyl residues of the constituents are oxidized.

2. The heparin fraction according to claim 1, wherein from about 25% to about 100% of hydroxyl residues of the constituents are oxidized.

3. The heparin fraction according to claim 2, wherein from about 50% to about 100% of hydroxyl residues of the constituents are oxidized.

4. The heparin fraction according to claim 3, wherein from about 90% to about 100% of hydroxyl residues of the constituents are oxidized.

5. The heparin fraction according to claim 1, wherein the constituents have a sulfate to carboxylate ratio ranging from about 2:1 to about 5:1.

43. A composition comprising from about 60% to about 100% of a heparin fraction consisting of constituents having molecular weights of from about 2,000 to about 4,000 daltons, wherein from about 1% to about 100% of hydroxyl residues of the constituents are oxidized, and from about 0% to about 40% of heparin, low molecular weight heparin, chondroitin sulfates, dermatan sulfates, heparan sulfates, heparin derivatives, or combinations thereof.

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FILE LAST UPDATED: 13 Jul 2005  (20050713/ED)

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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> d his full

     (FILE 'HOME' ENTERED AT 11:07:03 ON 14 JUL 2005)

     FILE 'REGISTRY' ENTERED AT 11:07:23 ON 14 JUL 2005
               E HEPARIN
               E HEPARIN/CN
               E HEPARAN/CN
L1           1 SEA ABB=ON  PLU=ON  HEPARAN/CN
               E HEPARIN/CN
L2           1 SEA ABB=ON  PLU=ON  HEPARIN/CN
               D SCAN
               D SCAN L1
L3        1265 SEA ABB=ON  PLU=ON  ?HEPAR!N?/CNS
L4        1058 SEA ABB=ON  PLU=ON  L3 NOT ?HEPAR!NASE?/CNS
L5           2 SEA ABB=ON  PLU=ON  L1 OR L2

     FILE 'REGISTRY' ENTERED AT 11:14:00 ON 14 JUL 2005
               D IDE L5 TOT

     FILE 'CAPLUS' ENTERED AT 11:15:39 ON 14 JUL 2005
               E MOUSA S/AU
L6         256 SEA ABB=ON  PLU=ON  ("MOUSA S"/AU OR "MOUSA S A"/AU OR "MOUSA
               S M A"/AU OR "MOUSA SHAKER"/AU OR "MOUSA SHAKER A"/AU OR
               "MOUSA SHAKER AHMED"/AU OR "MOUSA SHAKIR"/AU)
               E VASCULAR VISION/CS
               E VASCULAR VISION/PA
               E US2002-411851#/AP,PRN
L7           0 SEA ABB=ON  PLU=ON  US2002-411851#/AP,PRN
L8          33 SEA ABB=ON  PLU=ON  L6 AND (L4 OR L5)
               E MOLECULAR/CT
               E E106
               E E3+ALL
               E MASS/CT
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                E E3+ALL
L9          25097 SEA ABB=ON  PLU=ON  MASS+NT/CT OR MASS+NT/CT (L) MOL?
L10           122 SEA ABB=ON  PLU=ON  L9 AND (L4 OR L5)
L11            58 SEA ABB=ON  PLU=ON  L9 AND L5
L12             0 SEA ABB=ON  PLU=ON  L11 AND L6
L13          2743 SEA ABB=ON  PLU=ON  ((LOW OR HIGH) (2A) MOLECUL? (1A) (WEIGHT?
                OR MASS?)) AND L5
L14          1639 SEA ABB=ON  PLU=ON  ((LOW OR HIGH) (2A) MOLECUL? (1A) (WEIGHT?
                OR MASS?)) (L) L5
L15            15 SEA ABB=ON  PLU=ON  L14 AND L6
L*** DEL        0 S L15 AND OXIDI?
L*** DEL        8 S L14 AND OXIDI?
L16             9 SEA ABB=ON  PLU=ON  L14 AND ?OXIDI?
                D SCAN

      FILE 'CAPLUS' ENTERED AT 11:33:41 ON 14 JUL 2005


      FILE HOME

      FILE REGISTRY
      Property values tagged with IC are from the ZIC/VINITI data file
      provided by InfoChem.

      STRUCTURE FILE UPDATES:   13 JUL 2005  HIGHEST RN 854992-86-2
      DICTIONARY FILE UPDATES:  13 JUL 2005  HIGHEST RN 854992-86-2

      New CAS Information Use Policies, enter HELP USAGETERMS for details.

      TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

        Please note that search-term pricing does apply when
        conducting SmartSELECT searches.

      ************************************************************
      *                                                          *
      * The CA roles and document type information have been removed from *
      * the IDE default display format and the ED field has been added,   *
      * effective March 20, 2005.  A new display format, IDERL, is now    *
      * available and contains the CA role and document type information. *
      *                                                          *
      ************************************************************

      Crossover limits have been increased.  See HELP CROSSOVER for details.

      Experimental and calculated property data are now available. For more
      information enter HELP PROP at an arrow prompt in the file or refer
      to the file summary sheet on the web at:
      http://www.cas.org/ONLINE/DBSS/registryss.html

      FILE CAPLUS

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FILE COVERS 1907 - 14 Jul 2005 VOL 143 ISS 3
FILE LAST UPDATED: 13 Jul 2005 (20050713/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L16 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:968195 CAPLUS
DOCUMENT NUMBER: 140:246576
TITLE: Inhibition of Neointimal Proliferation in Balloon-Injured Arteries Using Non-Anticoagulant Heparin-Carrying Polystyrene
AUTHOR(S): Fujita, Masanori; Ishihara, Masayuki; Ono, Katsuaki; Matsumura, Koji; Saito, Yoshio; Yura, Hirofumi; Morimoto, Yuji; Shimizu, Masafumi; Takase, Bonpei; Ozaki, Shigeyuki; Kikuchi, Makoto; Maehara, Tadaaki
CORPORATE SOURCE: Department of Surgery II, National Defense Medical College, Saitama, Japan
SOURCE: Journal of Cardiovascular Pharmacology (2003), Volume Date 2004, 43(1), 31-38
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Non-anticoagulant heparin-carrying polystyrene (NAC-HCPS) has a higher activity to inhibit proliferation and migration of smooth muscle cells (SMCs) than heparin (Hep), periodate-**oxidized** (IO4-) Hep, and periodate-**oxidized** alkaline-degraded low mol. weight (IO4-LMW-) Hep. Less than 10 μg/mL of NAC-HCPS significantly inhibited the proliferation and migration of SMCs in vitro, while over 10-fold higher concns. of Hep, IO4-Hep, and IO4-LMW-Hep were required to obtain the same inhibition. On the other hand, neointimal growth (intimal cross-section area and intimal cross-section area/medial cross-section area ratio) in vivo following vascular injury 28 days after balloon denudation in a rat carotid artery was substantially inhibited with high dose of i.v. administration (total 30 mg) of resp. IO4-Hep, IO4-LMW-Hep, and NAC-HCPS. A low-dose (total 10 mg) administration of IO4-Hep and IO4-LMW-Hep did not prevent the neointimal growth when compared with the control; only NAC-HCPS (total 10 mg) was able to significantly inhibit the neointimal. Thus, NAC-HCPS has a more-than 10-fold larger activity to inhibit SMC activities such as proliferation and migration in vitro, when comparing with Hep, IO4-Hep, and IO4-LMW-Hep; NAC-HCPS also prevents neointimal growth in vivo at lower doses.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:769656 CAPLUS
DOCUMENT NUMBER: 137:280960
TITLE: Manufacture of low molecular weight heparin
INVENTOR(S): Murata, Hiroshi; Yatogo, Takemi
PATENT ASSIGNEE(S): Ito Ham Foods, Inc., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002293804	A2	20021009	JP 2001-93590	20010328

PRIORITY APPLN. INFO.: JP 2001-93590 20010328

AB The heparin having an anti-Xa activity/anti IIa activity ratio of >1.5, useful for chemical, cosmetic and pharmaceutical applications, etc., is obtained by chemical degrading a heparin solution having concentration of >10%, its swollen or slurry state, in the presence of an oxidant (H2O2) or reductant.

L16 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:794322 CAPLUS
DOCUMENT NUMBER: 132:18789
TITLE: Compositions and methods using an **oxidized** /reduced low-molecular-weight heparin compound for inhibiting thrombogenesis
INVENTOR(S): Hirsh, Jack; Weitz, Jeffrey I.
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Development Inc., Can.
SOURCE: U.S., 48 pp., Cont.-in-part of U.S. 5,763,427.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6001820	A	19991214	US 1997-870528	19970606
US 5744457	A	19980428	US 1995-540324	19951006
AU 9651400	A1	19961016	AU 1996-51400	19960329
US 5763427	A	19980609	US 1996-624327	19960329
JP 11506420	T2	19990608	JP 1996-528734	19960329
NO 9704500	A	19971128	NO 1997-4500	19970929

PRIORITY APPLN. INFO.:

US 1995-412332	B2	19950331
US 1995-540324	A2	19951006
US 1996-624327	A2	19960329
WO 1996-CA190	W	19960329

OTHER SOURCE(S): MARPAT 132:18789

AB Compns. and methods are provided for the treatment of cardiovascular diseases. More particularly, the invention relates to modifying thrombus formation by administering an agent which, inter alia, is capable of (1) selectively inactivating thrombin which is bound either to fibrin in a clot or to some other surface, but which has only minimal inhibitory activity against free thrombin, i.e., fluid-phase thrombin; (2) inhibiting the assembly of the intrinsic tenase complex, thereby inhibiting the activation of Factor X by Factor IXa; and (3) inhibiting the activation of Factor IX by Factor XIa. The compns. and methods of the present invention are particularly useful for preventing thrombosis in the circuit of cardiac bypass apparatus and in patients undergoing renal dialysis, and for treating patients suffering from or at risk of suffering from

thrombus-related cardiovascular conditions, such as unstable angina, acute myocardial infarction (heart attack), cerebrovascular accidents (stroke), pulmonary embolism, deep vein thrombosis, arterial thrombosis, etc. The invention uses a polyanionic carbohydrate, especially an **oxidized** /reduced low-mol.-weight heparin compound (preparation described).

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:397780 CAPLUS
DOCUMENT NUMBER: 129:58856
TITLE: Compositions and methods for inhibiting thrombogenesis
INVENTOR(S): Weitz, Jeffrey I.; Hirsh, Jack; Young, Edward
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Development Inc., Can.
SOURCE: U.S., 65 pp., Cont.-in-part of U. S. 5,744,457.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5763427	A	19980609	US 1996-624327	19960329
US 5744457	A	19980428	US 1995-540324	19951006
AU 9651400	A1	19961016	AU 1996-51400	19960329
JP 11506420	T2	19990608	JP 1996-528734	19960329
US 6001820	A	19991214	US 1997-870528	19970606
NO 9704500	A	19971128	NO 1997-4500	19970929
PRIORITY APPLN. INFO.:			US 1995-412332 B2	19950331
			US 1995-540324 A2	19951006
			US 1996-624327 A2	19960329
			WO 1996-CA190 W	19960329

OTHER SOURCE(S): MARPAT 129:58856
AB The present invention provides compns. and methods for inactivating thrombin bound to fibrin within a thrombus or clot, whereby the ability of clot-bound thrombin to catalytically promote further clot accretion is substantially diminished or eliminated. The compns. and methods of the present invention are particularly useful for preventing thrombosis in the circuit of cardiac bypass apparatus and in patients undergoing renal dialysis, and for treating patients suffering from or at risk of suffering from thrombus-related cardiovascular conditions, such as unstable angina, acute myocardial infarction (heart attack), cerebrovascular accidents (stroke), pulmonary embolism, deep vein thrombosis, arterial thrombosis, etc.
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:219836 CAPLUS
DOCUMENT NUMBER: 128:286337
TITLE: Processes for the preparation of low-affinity, low molecular weight heparins useful as antithrombotics
INVENTOR(S): Hirsh, Jack; Shaklee, Patrick N.; Knobloch, James E.; Weitz, Jeffrey I.; Young, Edward
PATENT ASSIGNEE(S): Hamilton Civic Hospitals Research Development Inc., Can.; Shaklee, Patrick N.; Knobloch, James E.; Weitz, Jeffrey I.; Young, Edward
SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9814481	A1	19980409	WO 1997-US17849	19971001
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5767269	A	19980616	US 1996-722408	19961001
AU 9747441	A1	19980424	AU 1997-47441	19971001
PRIORITY APPLN. INFO.:			US 1996-722408 A	19961001
			WO 1997-US17849 W	19971001

AB The present invention generally relates to processes for preparing low affinity, low mol. weight heparins (LA-LWM-heparins) which are endowed with pharmacol. and therapeutic properties that are surprisingly advantageous. In one embodiment, the process comprises: (1) nitrous acid depolymn. of unfractionated heparin to yield low mol. weight heparin (LMWH); (2) oxidation of the resulting LMWH to open the ring structures the nonsulfated uronic acid moieties using, for example, sodium periodate; and (3) reduction of the **oxidized** LMWH to reduce the aldehydes (to alcs.) formed during the depolymn. and oxidation steps using, for example, sodium borohydride. The resulting LA-LMW-heparins are capable of inactivating thrombin bound to fibrin within a thrombus or clot, whereby the ability of clot-bound thrombin to catalytically promote further clot accretion is substantially diminished or eliminated. As such, the resulting LA-LMW-heparins are useful for preventing thrombosis in the circuit of cardiac bypass apparatus and in patients undergoing renal dialysis, and for treating patients suffering from or at risk of suffering from thrombus-related cardiovascular conditions, such as unstable angina, acute myocardial infarction (heart attack), cerebrovascular accidents (stroke), pulmonary embolism, deep vein thrombosis, arterial thrombosis, etc.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:557633 CAPLUS
DOCUMENT NUMBER: 127:239118
TITLE: Drug delivery systems containing ester sunscreens and penetration enhancers
INVENTOR(S): Reed, Barry Leonard; Morgan, Timothy Matthias; Finnin, Barrie Charles
PATENT ASSIGNEE(S): Monash University, Australia; Reed, Barry Leonard; Morgan, Timothy Matthias; Finnin, Barrie Charles
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729735	A1	19970821	WO 1997-AU91	19970219
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2244089	AA	19970821	CA 1997-2244089	19970219
AU 9717134	A1	19970902	AU 1997-17134	19970219
AU 706967	B2	19990701		
EP 901368	A1	19990317	EP 1997-904304	19970219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000504697	T2	20000418	JP 1997-528834	19970219
US 6299900	B1	20011009	US 1998-125436	19981218
AU 9952589	A1	19991202	AU 1999-52589	19991001
US 2002028235	A1	20020307	US 2001-910780	20010724
US 6818226	B2	20041116		
US 2004013620	A1	20040122	US 2003-428016	20030502
US 2004013621	A1	20040122	US 2003-428019	20030502
US 6916487	B2	20050712		
US 2004028625	A1	20040212	US 2003-428012	20030502
US 6916486	B2	20050712		
US 2004028725	A1	20040212	US 2003-428018	20030502
US 2004096405	A1	20040520	US 2003-636976	20030808
US 2004081684	A1	20040429	US 2003-644085	20030820
US 2004146469	A1	20040729	US 2004-759303	20040120
PRIORITY APPLN. INFO.:			AU 1996-8144	A 19960219
			AU 1997-17134	A3 19970219
			WO 1997-AU91	W 19970219
			US 1998-125436	A3 19981218
			US 2001-910780	A2 20010724

OTHER SOURCE(S): MARPAT 127:239118

AB A transdermal drug delivery system which comprises at least one physiol. active agent or prodrug thereof and at least one dermal penetration enhancer; characterized in that the dermal penetration enhancer is a safe skin-tolerant ester sunscreen. A non-occlusive, percutaneous or transdermal drug delivery system which comprises: (1) an effective amount of at least one physiol. active agent or prodrug thereof; (2) at least one non-volatile dermal penetration enhancer; and (3) at least one volatile liquid; characterized in that the dermal penetration enhancer is adapted to transport the physiol. active agent across a dermal surface or mucosal membrane of an animal, including a human, when the volatile liquid evaps., to form a reservoir or depot of a mixture comprising the penetration enhancer and the physiol. active agent or prodrug within said surface or membrane; and the dermal penetration enhancer is of low toxicity to, and is tolerated by, the dermal surface or mucosal membrane of the animal. The mean flux of 2% ketoprofen in 70% volume/volume aqueous ethanol through shed snakes kinetics in presence of 2% octyl salicylate in 70% volume/volume aqueous ethanol was 27.66 as compared to 2.58 μg/cm2.h for azone. A transdermal aerosol contained 17β-estradiol 2, octyl dimethyl-p-aminobenzoate 8, ethanol 69, and di-Me ether 30%.

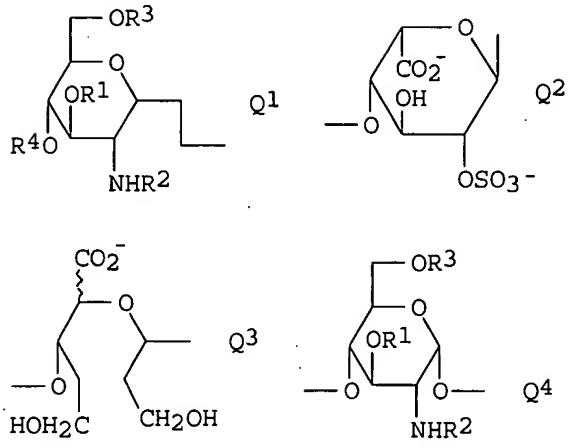
L16 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:413719 CAPLUS
DOCUMENT NUMBER: 127:92341
TITLE: Electrochemical oxidation and determination of heparin at electrodes modified with ruthenium oxide or copper oxide
AUTHOR(S): Lewinski, Krzysztof; Hu, Yun; Griffin, Charles C.; Cox, James A.
CORPORATE SOURCE: Dep. Chem., Miami Univ., Oxford, OH, 45056, USA
SOURCE: Electroanalysis (1997), 9(9), 675-679
CODEN: ELANEU; ISSN: 1040-0397
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The electrochem. oxidation of full-size heparin (13-15 kDa) is demonstrated in 1 M H3PO4 at a glassy carbon electrode coated with a ruthenium oxide film. The pathway apparently is analogous to chemical oxidation by periodate. By comparison to currents from inorg. species, it was apparent that only about 2 electrons per mol were involved. Flow-injection anal. (FIA) allowed detns. down to 2 μM heparin, but the calibration plot was nonlinear. Low mol. weight heparin (5-6 kDa) was not electroactive with this system. In basic solution at a glassy carbon electrode that was modified with a film of Cu2O, both full-size and low mol. weight heparin were **oxidized.** The pathways involved oxidative desulfation and attack on saccharide units with evolution of CO2. Linear calibration plots which extended into the sub-μM level were obtained by FIA. The detection limits (3σ) were 9 nM for full-size and 20-30 nM for various low mol. weight heparin samples.

L16 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:417717 CAPLUS
DOCUMENT NUMBER: 111:17717
TITLE: Low-molecular-weight heparins with a regular structure, their preparation and biological uses
INVENTOR(S): Lormeau, Jean Claude; Petitou, Maurice; Choay, Jean; SANOFI
PATENT ASSIGNEE(S): SANOFI, Fr.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 287477	A2	19881019	EP 1988-400928	19880415
EP 287477	A3	19890726		
EP 287477	B1	19941102		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2614026	A1	19881021	FR 1987-5457	19870416
FR 2614026	B1	19920417		
FI 8801783	A	19881017	FI 1988-1783	19880415
FI 88046	B	19921215		
FI 88046	C	19930325		
NO 8801660	A	19881017	NO 1988-1660	19880415
NO 170940	B	19920921		
NO 170940	C	19921230		
AU 8814663	A1	19881020	AU 1988-14663	19880415

AU 601566	B2	19900913		
JP 63278901	A2	19881116	JP 1988-91891	19880415
ZA 8802662	A	19881130	ZA 1988-2662	19880415
US 4990502	A	19910205	US 1988-181969	19880415
CA 1327968	A1	19940322	CA 1988-564296	19880415
DK 8802103	A	19881017	DK 1988-2103	19880418
DK 173982	B1	20020325		
PRIORITY APPLN. INFO.:			FR 1987-5457 A	19870416

GI



AB A low-mol.-weight heparin, R(XY)nR' [I; R = H, Q1; X = Q2, Q3; Y = Q4; R1 = H, SO3-; R2 = Ac, SO3- (.apprx.90%); R3 = H, SO3- (.apprx.70%); R4 = H, uronic acid; R' = H, natural uronic acid, **oxidized** uronic acid with aldehyde groups reduced to alcs.; n = 7-15], of .apprx.4800-9000 mol. weight, is prepared by (1) treating an aqueous solution of heparin (0.5-5%, weight/volume) with HIO4 (0.5-4%, weight/volume) at pH 4.5-6.5 and 0-10°; (2) treating the heparin chains obtained with 0.1-0.3N strong base; (3) treating the depolymd. fragments with a reducing agent; (4) eliminating the excess reducing agent and precipitating the fragments with a mineral salt and an alc.; (5) recovering the product and converting it to a pharmaceutically acceptable salt. I does not have anticoagulant activity and is useful as a medicament for regulating certain physiol. systems. Porcine heparin Na salt (10 g) was treated with NaIO4 at pH 5.0 and 4° for 24 h in the dark, the residual IO4- was removed by dialysis, and the modified heparin was depolymd. with 10N soda for 3 h at 18-21°. The product was reduced with NaBH4 and then fractionated by repeated precipitation with NaCl-containing EtOH, to give 5.0 g product (IC 1772). IC 1772 inhibited the proliferation of rat smooth muscle cells in vitro and in vivo similarly to heparin standard, inhibited the formation of complement C 3b-protein B complex with a 50% inhibitory concentration of 0.4 μg/mL (heparin value = 0.5 μg/mL), and administered i.v. to rabbits at 1 mg/kg had antithrombotic activity in all 10 animals.

L16 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
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AU 8310331	A1	19840126	AU 1983-10331	19830112
JP 59020302	A2	19840202	JP 1983-3271	19830112
JP 04042401	B4	19920713		
EP 101141	A2	19840222	EP 1983-300155	19830112
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ES 519015	A1	19840201	ES 1983-519015	19830114
DK 8303255	A	19840120	DK 1983-3255	19830714
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AB Low mol. weight heparin fractions were prepared by acidifying normal heparin to pH .apprx.3-5 to give heparinic acid (I) and depolymg. I by heating in the presence of an **oxidizing** agent, e.g., H2O2, to give heparin fractions of .apprx.4,000-12,000 Dalton. The low mol. weight heparin fractions prepared have a ratio of antithrombotic activity to anticoagulant activity which is superior to that of the normal heparin (no data).